



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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C07K 14/39, C12N 9/12, C12Q 1/02

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US

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(81) Designated States: AU, CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published

With international search report.

(88) Date of publication of the international search report:

26 October 2000 (26.10.00)

(54) Title: SCREENING METHODS BASED ON THE USE OF PROTEIN KINASES

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PDK1      84  FGRILGEGSPSTVVLAEIATSRREYAIKILEKQIIRKQVYVTRERDYMRLI--EPPVKLYETFOOD--LYECUSYAK 163
DSTPK61   164  FGRILGEGSYSTVVLAVDIESRREYAIKVCERKILIRRKQVYIRREREVHOMVNVGPFVNLSCTFODQNSLYFVMYYAK 246
Pkh1      127  FGRILGEGSYSTVVLATAISORRYAVKVLSEYLIIRKKVKYVTVVERKALOKLNGTAGIKLFFTFODEASLYFLEYAP 207
Pkh2      181  FGRVIGDGAYSTVMLATSIDTKRYAVKVLSEYLIIRKKVKYVTEIETALOKLNSSTVVRLETFODEASLYFLEYAP 261

PDK1      164  NGELDAYIRKIGSDETCARFYLAATVSALEYLHONGIHRDLKPNENILLNEDMHICITDFGTAKVLS----- 231
DSTPK61   245  NGDLPYIIRVGSQVACREYAAFLPLACE--MH--REVVRDLKPNENILLDEDMHITIDFGSAKVITABERALATERCSE 325
Pkh1      208  EGDPLQIKKYGSNETCARYYASCIIDAVDSLHNGIHRDIKPNENILLDNEKVKLTDFGTAKILVE----- 276
Pkh2      262  NGDPLQMKKYGSDETCARYYAACIIDAYDLHSEGLIHRDIKPNENILLDCEMKIKLTDFGTAKILN----- 329

PDK1      232  -----PESKQ-----ARASFVGTATVSPPELLQKSAKSS 262
DSTPK61   326  QRRENSDEDDQSDALNEDDITDRDSKELDDRDGQCCQEL--DSPRRQRAYTGERKASFVGTATVSPVELQKQPTPA 406
Pkh1      277  -----EPSTADGRFYFDLARSKSFVGTATVSPPELLNDYTD--R 317
Pkh2      330  -----PTRKSVSKPYDLSTRSKSFVGTATVSPPELLNDSTETR 369

PDK1      263  SLDLWAGCIIYQLVAGPPFRAGNEYLIPOKIIKLEYDFVLSSTVYARDLVKLLVLAATRRLGQPE--GYGP--LKAHPF 341
DSTPK61   407  SLDLWAGCIIYQNIAGPPFRGNDYVIFEN--LLDCAVLEPPGGRDADA--DLVRKLLKVDPRDLCAQDRTGYTSIRAHPF 486
Pkh1      318  CDIWAAGCIIYQILAGPPFRAGNEYLIPOKVKIKIYQFTAGFPCLIVKDLVKLLVDPNDRL-----TINQIKAHFF 390
Pkh2      370  CDIWAAGCIILOMIAGPPFRAGNEYLIPOKVMKVOYQFTGFPCLIVKDLVKLLVDPNDRL-----TISQIKAHFF 442
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(57) Abstract

A method of identifying a compound which inhibits to different extents (a) a host yeast cell protein kinase or kinases and (b) a protein kinase derivable from a source other than the said host yeast cell that is equivalent to the said host yeast cell protein kinase or kinases, wherein a compound is exposed to 1) a first host yeast cell wherein the yeast cell is capable of expressing the said host yeast cell protein kinase or kinases and is not capable of expressing the said equivalent protein kinase and 2) a second host yeast cell wherein the yeast cell is (a) not capable of expressing the said yeast cell protein kinase or kinases and (b) is capable of expressing the said equivalent protein kinase derivable from a source other than the host yeast cell and the effect of the compound on the viability of the said yeast cells is measured, and a compound that affects the viability of the first said yeast cell and the said second yeast cell differently, is identified. The method may be useful in a screen for identifying compounds that inhibit a mammalian or fungal protein kinase. The compounds may be useful in medicine.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/04228

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/39 C12N9/12 C12Q1/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMFUN 'Online! EMBL, Heidelberg Accession Number Z74842 (Y13140), 9 July 1996 (1996-07-09) DURAND P. ET AL.: "S. cerevisiae chomosome XV reading frame ORF YOL100w" XP002138494 abstract	44
X	DATABASE TREMBL 'Online! EMBL, Heidelberg Accession Number Q03407 (S. cerevisiae; pkinase), 1 November 1996 (1996-11-01) DIETRICH F.S. ET AL. : "Sequence from N.A. " XP002138495 abstract	44

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

30 May 2000

Date of mailing of the international search report

20.06.00

Name and mailing address of the ISA

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Authorized officer

Luzzatto, E

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/04228

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	R.A.MAURER: "Isolation of a yeast protein kinase gene by screening with a mammalian protein kinase cDNA" DNA, vol. 7, 1988, pages 469-474, XP000886952 cited in the application the whole document ---	24-26
X	WO 94 23039 A (CANCER RES INST ROYAL ;MARSHALL CHRISTOPHER JOHN (GB); ASHWORTH AL) 13 October 1994 (1994-10-13) abstract; examples 4,5 page 4, line 1 - line 12 page 6, line 28 -page 11, line 23; claims ---	1
X	CHEN, PING ET AL: "A pair of putative protein kinase genes (YPK1 and YPK2) is required for cell growth in Saccharomyces cerevisiae." MOLECULAR & GENERAL GENETICS, (1993) VOL. 238, NO. 2-3, PP. 443-447. , XP000887391 the whole document ---	28-30
X	KUBO K. ET AL.: "A novel yeast gene coding for a putative protein kinase" GENE, vol. 76, 1989, pages 177-180, XP000887394 cited in the application the whole document ---	24-26
X	E. BILSLAND ET AL.: "Yeast functional analysis report" YEAST, vol. 14, no. 7, May 1998 (1998-05), pages 655-664, XP000909706 UK the whole document ---	13,14, 17-19
A	US 5 789 184 A (MANFREDI JOHN ET AL) 4 August 1998 (1998-08-04) column 7, line 50 -column 10, line 59 ---	1
A	EP 0 861 896 A (DADE BEHRING MARBURG GMBH) 2 September 1998 (1998-09-02) the whole document ---	28-34
A	WO 98 41638 A (MEDICAL RES COUNCIL) 24 September 1998 (1998-09-24) page 79, line 25 -page 81, line 14; claims; examples 6-14 ---	32

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/04228

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ALESSI D R ET AL: "3-PHOSPHOINOSITIDE-DEPENDENT PROTEIN KINASE-1 (PK1): STRUCTURAL AND FUNCTIONAL HOMOLOGY WITH THE DROSOPHILA DSTPK61 KINASE" CURRENT BIOLOGY,GB,CURRENT SCIENCE,, vol. 7, no. 10, 1 October 1997 (1997-10-01), pages 776-789, XP002070054 ISSN: 0960-9822 the whole document ----	34
P,X	CASAMAYOR A ET AL: "Functional counterparts of mammalian protein kinases PK1 and SGK in budding yeast." CURRENT BIOLOGY, (1999 FEB 25) 9 (4) 186-97. , XP000909655 -----	13-19, 28-30, 33,34, 44-48

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 99/04228

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 27, 35, 37-43
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box 1.2

Claims Nos.: 27,35,37-43

Claims 35 does not relate in a clear and unambiguous way to any technical feature which could allow a meaningful search with respect to the claimed kit to be carried out.

Claims 38-43 relate to a completely undefined subject-matter, since no compounds which could fall within the scope of the said claims have been disclosed in the application. Hence, no technical feature can be identified on which a meaningful search could be based.

Claim 37 relates to a protein kinase solely defined by its being novel; hence, no technical features are to be found in this claim which could provide a basis for a search.

Claim 44 relates to pure polypeptides encoded by an *S. cerevisiae* ORF which, however, are not defined by a sequence in a searchable format: the search has thus been carried out on the basis of *S. cerevisiae* sequences provided in the sequence listing, namely SEQ ID 42 and 48. The same applies to claims 45-49 which are, directly or indirectly, dependent on claim 44.

Claims 33 and 34 have been searched only insofar as related to the use of Pkh1/2 or PDK1 respectively to phosphorylate any protein, except (for PDK1) PKBalpha and p70S6 kinase, in view of the fact that the expression "suitable variant, fragment, derivative or fusion thereof..." appears to encompass any possible protein. This interpretation of the said expression is suggested by the disclaimer relating to proteins not directly related to Ypk1, Ypk2 or SGK as PKBalpha and p70S6. The undefined meaning of the said expression renders also a meaningful search with respect to the subject-matter of claim 27 impossible.

The invention is based on the discovery of two yeast equivalents of PDK1, namely Pkh1 and Pkh2: no other such equivalents are disclosed in the application or can be meaningfully searched. Hence, claim 11 has been searched only insofar as limited to Pkh1 and Pkh2 as functional equivalents of PDK1.

The invention is further based on the discovery that the yeast proteins Ypk1 and Ykr2 are the functional equivalents of the human protein kinase SGK. This is the contribution over the prior art that the invention could be seen as providing. No other such functional equivalents are disclosed in the application or can be searched for in a meaningful way. The search with respect to the subject-matter of claim 12, therefore, has been limited to a method wherein the yeast cell is incapable of expressing Ypk1 and/or Ykr2 and is capable of expressing SGK.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/04228

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9423039 A	13-10-1994	AU 677834 B	08-05-1997
		AU 6382394 A	24-10-1994
		CA 2157774 A	13-10-1994
		EP 0703984 A	03-04-1996
		JP 9501302 T	10-02-1997
		US 5958721 A	28-09-1999
		AU 696939 B	24-09-1998
		AU 1586195 A	29-08-1995
		CA 2182967 A	17-08-1995
		EP 0742827 A	20-11-1996
		WO 9521923 A	17-08-1995
		JP 9508795 T	09-09-1997
US 5789184 A	04-08-1998	US 5876951 A	02-03-1999
		AU 6354198 A	09-07-1998
		AU 685103 B	15-01-1998
		AU 6490994 A	24-10-1994
		CA 2158274 A	13-10-1994
		EP 0692025 A	17-01-1996
		EP 0915154 A	12-05-1999
		JP 8510115 T	29-10-1996
		WO 9423025 A	13-10-1994
EP 0861896 A	02-09-1998	DE 19708173 A	03-09-1998
		CA 2224404 A	28-08-1998
		JP 10248566 A	22-09-1998
WO 9841638 A	24-09-1998	AU 6412498 A	12-10-1998
		EP 0983363 A	08-03-2000

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

MILES, John, S.
Eric Potter Clarkson
Park View House
58 The Ropewalk
Nottingham NG1 5DD
ROYAUME-UNI

Date of mailing (day/month/year) 17 May 2000 (17.05.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference MEDY/P22233PC	
International application No. PCT/GB99/04228	International filing date (day/month/year) 14 December 1999 (14.12.99)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input checked="" type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address	State of Nationality	State of Residence
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	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence
Name and Address TORRANCE, Pamela Diane 1814 Hearst Avenue, #D Berkeley, CA 94703 United States of America	State of Nationality US	State of Residence US
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PATENT COOPERATION TREATY

PCT/GB99/0422

PCT 3

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(PCT Rule 92bis.1 and
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To:

MILES, John, S.
Eric Potter Clarkson
Park View House
58 The Ropewalk
Nottingham NG1 5DD
ROYAUME-UNI

Date of mailing (day/month/year)

17 May 2000 (17.05.00)

Applicant's or agent's file reference

MEDY/P22233PC

International application No.

PCT/GB99/04228

International filing date (day/month/year)

14 December 1999 (14.12.99)

IMPORTANT NOTIFICATION

1. The following indications appeared on record concerning:

☒

the applicant

☒

the inventor

☐

the agent

☐

the common representative

Name and Address

THORNER, Jeremy, William
701 Arlington Avenue
Berkeley, CA 94707-1633
United States of America

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

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the person

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the name

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the address

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the nationality

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the residence

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State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

The above is now recorded as applicant/inventor for the United States of America only

4. A copy of this notification has been sent to:

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the receiving Office

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the designated Offices concerned

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the International Searching Authority

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the elected Offices concerned

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the International Preliminary Examining Authority

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other:

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PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

MILES, John, S.
Eric Potter Clarkson
Park View House
58 The Ropewalk
Nottingham NG1 5DD
ROYAUME-UNI

Date of mailing (day/month/year)
17 May 2000 (17.05.00)

Applicant's or agent's file reference
MEDY/P22233PC

International application No.
PCT/GB99/04228

IMPORTANT NOTIFICATION

International filing date (day/month/year)
14 December 1999 (14.12.99)

1. The following indications appeared on record concerning:



the applicant



the inventor



the agent



the common representative

Name and Address

State of Nationality

State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:



the person



the name



the address



the nationality



the residence

Name and Address

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91 Clark Street
New Haven
CT 06511
United States of America

State of Nationality

ES

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

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The above person has been added as applicant/inventor for the United States of America only

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

To:

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Park View House
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09 JAN 2001

Date of mailing
(day/month/year)

02.01.2001

Applicant's or agent's file reference
MEDY/P22233PC

IMPORTANT NOTIFICATION

International application No.
PCT/GB99/04228

International filing date (day/month/year)
14/12/1999

Priority date (day/month/year)
14/12/1998

Applicant

THORNER, Jeremy William et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference MEDY/P22233PC	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB99/04228	International filing date (day/month/year) 14/12/1999	Priority date (day/month/year) 14/12/1998
International Patent Classification (IPC) or national classification and IPC C12Q1/00		
Applicant THORNER, Jeremy William et al.		



1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 14 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 10/07/2000	Date of completion of this report 02.01.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Luzzatto, E Telephone No. +49 89 2399 8169 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/04228

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

Description, pages:

1-123 as originally filed

Claims, No.:

1-30,32-49 as originally filed

Drawings, sheets:

1-19 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/04228

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 7-9,15,23,27,31-43.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 33,34,36 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☒ the claims, or said claims Nos. 7-9,15,23,28,32 are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 27,31,35,37-43.

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims 1-6,10-12,16,20-22,47,49

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/04228

	No:	Claims	13,14,17-19,24-26,28-30,44-46,48
Inventive step (IS)	Yes:	Claims	11,12,16,20-22
	No:	Claims	1-6,10,13,14,17-19,24-26,28-30,44-49
Industrial applicability (IA)	Yes:	Claims	1-6,10-14,16-22,24-26,28-30,44-49
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/04228

Re Item I

Basis of the opinion

- 1) Sequence listing pages 1-39 filed with the letter of 12.4.2000 do not form part of the application (Rule 13^{ter}.1(f) PCT).

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

- 1) Claims 27, 35, 37-43 have not been searched: their subject-matter therefore has not been examined (R. 66.1(e) PCT) (see also part VIII hereinbelow).
- 2) Claims 7-9, 15, 23, 28, 32-34 has not been examined in view of lack of support (Art. 6) (see item VIII hereinbelow).
- 3) Claims 33, 34 and 36 has not been examined for lack of clarity (see item VIII.8 hereinbelow).
- 4) Claim 31 is not to be found in the claims on file.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: DNA, 469-474, 1988
- D2: Mol.Gen. Genet., 443-447, 1993
- D3: Gene, 177-180, 1989
- D4: Emfun (EMBL), Acc. Number Z74842
- D5: Trembl (EMBL), Acc. Number Q03407)
- D6: Yeast, 655-664, 5/98
- D7: WO-A-9423039

- 1) The present application does not meet the requirements of Art. 33(2) PCT due to lack of novelty.
 - 1.1) D1 (DNA, Maurer et al.) and D2 (Chen et al., MGG) disclose the Ypk1 protein kinase, which is capable of phosphorylating the polypeptide defined in claim 24 as well as being phosphorylated by Pkh1 or Pkh2 or PDK1. D1 and D2, therefore, anticipate the subject-matter of claims 24-26.
D3 (Gene, Kubo et al.) discloses the yeast YKR2 protein kinase. Also this document, thus, anticipates the subject-matter of claims 24-26.
 - 1.2) D4 (Z74842) and D5 (Q03407) disclose the polypeptide encoded by the ORF YOL100w and that having the sequence designated in the application as SEQ ID 47 (p. 15, l. 20-p. 16, l. 6 of the description) respectively, thus anticipating the subject-matter of claims 44, 45 and 48 (as to the latter, it should be noted that for the assessment of novelty what matters are the actual features of the product, independent of the way in which the product has been obtained).
 - 1.3) D2 discloses *S. cerevisiae* mutants unable to express functional Ypk1 or Ypk2 kinases. It thus anticipates the subject-matter of claims 28-30 (see also item VIII.9 hereinbelow).
 - 1.4) D6 (Yeast, Bisland et al.) discloses yeast cells whose ORF YOL100w has been disrupted by insertion of a selectable marker (see abstract, Material and Methods, chapter "Genomic disruptions", fig.1, p. 662, left-hand col., l. 9-p. 663, right-hand col., l. 31). It also discloses the transformation of cells with the entire disruption insert (see chapter "plasmid construction" starting on p. 658).
D6, thus, anticipates the subject-matter of claims 13, 14, 17-19, 46.
- 2) The present application does not meet the requirements of Art. 33(3) PCT due to lack of an inventive step.
 - 2.1) D7 (WO-A-9423039) is considered to represent the closest prior art.
It discloses a screening method for an inhibitor of a mammalian protein kinase

(PK) comprising the transformation of a yeast cell (e.g. *S. pombe*) with the mammalian gene coding for the said PK, wherein the yeast cell is incapable of expressing the yeast gene equivalent to the mammalian PK (see passages cited in the Search Report). As clearly shown by examples 4 and 5, the screening method comprises the use of the aforescribed transformed strain along with a non-transformed control strain (which corresponds to the "first host cell" to which claim 1 relates).

Hence, the sole difference between the method of D7 and that of claim 1 is that the latter excludes the use of a mammalian gene for transformation or uses a pathogenic yeast.

However, absent any indication whatsoever as to an unexpected effect linked to the use of a non-mammalian gene/pathogenic yeast or as to e.g. a prejudice in the art which would have prevented the skilled person from extending the teaching of D7 to non-mammalian genes or to pathogenic yeasts, the subject-matter of claims 1 and 2 appears to be the mere result of the customary practice of the skilled person.

Moreover, it is not even clear which (if any) is the technical problem solved by the general methods of claims 1 and 2; a screening assay for the identification of a compound should be based on the clear identification of a target molecule, thus allowing the identification of specific compounds which affect the said target. In the present case, no such target is defined: the general class of protein kinase is too broad to be considered as a specific target.

Claims 1 and 2, thus, lacks an inventive step.

Even if this objection had been overcome, the claims would have still offended against Art. 5 and 6 (see part VIII.1 hereinbelow).

2.2) Dependent claims 3-5, 10 relate to well known yeast species and well known features and thus lack an inventive step (art. 33(3) PCT).

2.3) Claim 6 relates to Pkh1 and Pkh2, which are not disclosed in the prior and, if the objection under Art. 6 had been overcome (see item VIII hereinbelow), would have thus been novel (Art. 33(2) PCT).

However, an inventive step cannot be acknowledged for this claim, in view of the fact that Pkh1 and Pkh2 are the products of well known ORFs, which were known to code for PK. Hence, the mere use of known PK in a conventional assay is not

inventive.

2.3) No opinion can be given as to the novelty and inventive step of subject-matter of claims 7-9 (see item VIII hereinbelow).

2.4) If the clarity objection had been overcome (see item VIII hereinbelow) by limiting claims 11 and 12 to the systems (Pkh1+Pkh2)/PDK1 and (Ykp1 +Ykr2)/SGK, the subject-matter of these claims could have met the requirements of Art. 33 PCT since none of the documents cited in the Search Report discloses or suggests the functional equivalence of the two said pairs of proteins and PDK1 and SGK. Thus, assays for the identification of compounds based on these systems are neither disclosed nor suggested in the available prior art.

2.5) Claim 16 appears to meet the requirements of Art. 33 PCT (see however part VIII hereinbelow), since, absent any indication in the prior art as to the relatedness of Pkh1 and Pkh2 with PDK1, the skilled person would have had no incentive to produce a cell as claimed.

For the same reasons, claims 20, 21 and 22 appear to meet the requirements of Art. 33 PCT.

As to claim 23, an opinion as to novelty and inventive step could only have been given if the objection under Art. 5 and 6 PCT (see item VIII) had been overcome.

2.6) If the clarity objection had been overcome (see item VIII.1) by suitably limiting its subject-matter, claim 32 would lack an inventive step, because Ypk1 and Ykr2 are known PK and their substrates are known. The amended claim would be rendered novel by the disclaimer relating to SGK, PKB α and p70S6 kinase. However no inventive step could be acknowledged in view of the absence of any unexpected feature in the mere extension of known assays to the general class to which the known substrates belong.

2.7) If the clarity objection had been overcome (see item VIII) by clearly and unambiguously relating claim 33 to the proteins actually disclosed in the application, i.e. Pkh1 and Pkh2, the claimed subject-matter could have possibly met the requirements of Art. 33 PCT.

The same line of arguments applies to claim 34, which could have met the

requirements of Art. 33 PCT if **clearly and unambiguously** related to the use of PDK1 to phosphorylate Ypk1, Ykr2 or SGK.

- 2.8) In view of the fact that the polypeptides encoded by the ORF yol100w and YDR490c are known, as well as their function, no inventive step can be acknowledged for the subject-matter of claim 47 and 49. As to claim 49, this conclusion is further reinforced by the the absence of any indication that such an antibody has been obtained and, hence, of any unexpected features thereof.
- 3) The document CASAMAYOR A ET AL: Functional counterparts of mammalian protein kinases PDK1 and SGK in budding yeast.' CURRENT BIOLOGY, (1999 FEB 25) 9 (4) 186-97. , XP000909655 could become relevant should the priority of the present application not be valid.

Re Item VII

Certain defects in the international application

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D7 is not mentioned in the description, nor are these documents identified therein.

Re Item VIII

Certain observations on the international application

- 1) The claims lack clarity (Art. 6 PCT) due to the use of the term "equivalent" in the following context "...protein kinase... **equivalent to the said host yeast cell protein kinase...**", because it is not possible for the skilled person to clearly and unambiguously understand the meaning of the term "equivalent". The description provides a definition of the said term (p. 6), however it falls short of describing a test capable of identifying, **clearly and unambiguously**, a protein kinase equivalent to another one. This is especially true in view of the fact that protein kinase have a plethora of effects, and thus each single PK would require a specific test.
- This inherent ambiguity of the claimed method is also shown by the fact that claim

6 relates to Pkh1 or Pkh2 as the host yeast cell protein kinase to be used in the method of claim 1; however, as clearly disclosed in the application (p. 78, l. 15-p. 79, l. 12) single deletion mutants (pkh1 Δ and pkh2 Δ) are viable and grow indistinguishably from congenic PKH1⁺ and PKH2⁺ (see D8, p. 187, right-hand col., first full par.). The same applies to Ypk1 and Ykr2 (see aforementioned passages and p. 87-88).

Hence, the skilled person, on the basis of the application, is not even in the condition to come to the conclusion that Pkh1 or Pkh2 are functional equivalents of PDK1: he can only apparently conclude that **both** said proteins, considered as a single system, are equivalent to PDK1. The same applies to Ypk1 and Ykr2 with respect to SGK. Concerning PKB, the description states that only very high expression levels of the said protein could rescue inviable ypk Δ ykr2 Δ (p. 78, l. 23-27, p. 89, l. 2-5) and provides no indication that such a protein would be suitable for the claimed assay.

Claims 1 and 2 are thus unclear because the expression "functional equivalent" is vague.

The same applies to claims 13,15,16,18,19,28-30,32-34.

- 2) Moreover, the said claims contravene Art. 6 for lack of support and their subject-matter contravenes Art. 5 since a suitable test for determining a functional equivalent of any given protein kinase valid for the whole breadth of the claims is not disclosed in the application. The skilled person is only capable of reproducing the claimed method insofar as related to the systems (Pkh1 and Pkh2)/PDK1 and (Ypk1 and Ykr2)/SGK.

The absence of any indication as to the said equivalents entails that no opinion can be given as to novelty and inventive step for the subject-matter of claim 32, since such an opinion could only be limited to Ypk1 and Ykr2.

It should be stressed that the contribution the invention allegedly makes over the prior art is to be seen in the identification of the kinases Pkh1 and Pkh2 as functional equivalents of PDK1 and of Ypk1 and Ykr2 of SGK. In the present case, therefore, claims whose subject-matter does not directly relate to the said proteins would amount to an unwarranted extension of protection.

- 3) No Pkh1 and Pkh2/Ypk1 and Ykr2 pathogenic yeast equivalents are described in the application: example 4 allegedly relates to the "identification of Candida

genes" related to these genes, but it merely discloses fragments of three Candida genes which appear to be closely related thereto: no data of any kind (not even the full length sequence) are provided which could support the contention that the said equivalents have actually been identified. Example 4, therefore, merely indicates that said equivalents **could be found**. Hence, also concerning the use of pathogenic yeast in the claimed methods, the application contravenes Art. 5 and the claims lack support (Art. 6 PCT).

- 4) The polypeptide Pkh1 is defined as having the sequence designated SEQ ID 47 whereas Pkh2 is encoded by the sequence SEQ ID 42. No other yeast equivalent proteins are described in the application.
Hence all claims relating to undefined equivalent ORFs of Pkh1 and Pkh2 (namely cl. 6, 26 44 and claims directly or indirectly dependent thereon) should have been amended by deleting any reference thereto, in order for them to comply with the requirements of Art. 6 (support) and 5 PCT.
- 5) Claims 24 and 25 are unclear (Art. 6 PCT). The fact that kinases may have a higher phosphorylating efficiency for a certain sequence or a certain protein than for others does not necessarily entail that they are not capable to phosphorylate different substrates, albeit with a lower efficiency. Hence, claims 24 and 25 do not allow a clear and unambiguous definition of the matter for which protection is sought, in view of the fact that known kinases might well phosphorylate the substrates to which the claims relate.
The said claims should have thus been amended by introducing clear technical features of the claimed protein.
- 6) Claim 35 does not relate to any technical feature and contravenes therefore Art. 6 PCT for lack of clarity.
- 7) Claim 36 is dependent on claim 35 and relates to "said yeast cell protein...". It is thus unclear (Art. 6 PCT) since claim 35 does not relate to any protein kinase. Hence, since also claim 35 and claims 1 and 2 are unclear, claim 36 is so unclear that no opinion can be given as to novelty and inventive step.
- 8) Claims 33 and 34 are unclear (Art. 6 PCT) in view of the fact that the expression

"suitable variant, fragment, derivative or fusion thereof..." appears to encompass any possible protein, even not directly related to Ypk1, Ypk2 or SGK, such as PKB α and p70S6 kinase. Hence, since this expression is also used in combination with Pkh1/2 and PDK1 respectively, the claims do not clearly define either the phosphorylating or the phosphorylated agent, thus rendering impossible a clear definition of the matter for which protection is sought.

The same applies to claims 47 and 48, which can only be examined insofar as related to Pkh1 and Pkh2, i.e. to the products of the ORFs YOL100w and YDR490c.

- 9) The same argument set out as to claim 34 applies to claim 44, which thus also lacks clarity.

Moreover, claim 44 also lacks clarity due to the expression "equivalent ORF" which leaves the skilled person at a loss as to the exact scope of the claim. Claim 44 contravenes Art. 6 PCT also for lack of support, in view of the fact that it is only with undue burden that the skilled person could find out which, if any, ORFs are equivalent to the *S. Cerevisiae* ORFs to which the claim relates. That this task is no obvious one, is shown by one of the main basis for the present invention, i.e. the characterisation of the protein products (Pkh1 and Pkh2) encoded by a **known** ORF (see p. 91, l. 25-p. 92, l. 7 of the description). The same objection applies of course to claims 45-49 which are, directly or indirectly, dependent on claim 44.

- 10) Claims 37-43 are unclear in that they do not relate to any technical feature of the claimed compounds and should be thus deleted.

- 11) The lack of definite meaning of the expression "variant, derivative, fragment..." discussed in hereinabove renders fully unclear the scope of claim 27, which should thus be deleted.

- 12) The subject-matter of claim 30 is unclear for the following reasons:
- the expression "for example" renders the three proteins which follow it in the claim completely non-limiting, hence rendering the meaning of the claim fully unclear (see Guidelines, III, 4.6);
Moreover, the claim and its subject-matter contravene A. 6 (lack of support) and

Art. 5 PCT respectively, in that the skilled person could reproduce the invention without undue burden only insofar as related to exemplified proteins, namely SGK, Ypk1, Ykr2. The description itself states that "such a method **may be used for the identification of a functional homologue of Ypk1 or Ykr2...**" (p. 54, l. 19-20), thus indicating that no such homologues are known.

- 13) Claim 32 lacks support (Art. 6 PCT) for the same reasons set out with respect to claim 30.
- 14) Even if claim 30 was interpreted by not taking into account the expression "for example", it contravenes in any case Art. 6 for lack of clarity, in that its subject-matter is broader than that of claims 28 and 29, on which it should depend (see Guidelines, III, 3.4-3.5).
- 15) Claim 1 is unclear (Art. 6 PCT) because the expression "pathogenic yeast" is meaningful only if the organism for which the yeast is pathogenic is defined.
- 16) Claim 11 is unclear (Art. 6 PCT) because the terms Pkh1 and Pkh2 are in brackets (point 1) and 2)), thus allowing the interpretation that they are but an example of a functional equivalent of PDK1. However, they are the only such equivalents known and the contribution the invention allegedly makes over the prior art is based on this very discovery. Hence, the claim should have been amended by clearly relating it to yeast cells incapable of expressing the Pkh1 and Pkh2 proteins, thus dispelling any doubt as to the meaning of the expression "functional equivalent of human PDK1".
- 15) Claim 14 is unclear, since Pkh1 and Pkh2 relate to well defined *S.cerevisiae* protein kinases, and no other proteins with this denomination appear to have been described in the prior art or in the application. Hence, the expression "...**endogenous** Pkh1 and/or Pkh2..." should have been deleted since it appears to entail that various Pkh1 and Pkh2 proteins are known.
- 16) The sequence designations to be found on p. 47, l. 23, 44, l. 21 are unclear. They should have been either clarified in their meaning or been deleted.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/04228

- 17) Claims 23 lacks support (Art. 6 PCT) and its subject-matter contravenes Art. 5 PCT since no further yeast equivalents of PDK1 are disclosed besides Pkh1 and Pkh2, especially no Candida equivalents. The said claim should have thus been deleted.
- 18) Claims 7-9, 15, 28, 30 lack support (Art. 6) and their subject-matter contravenes Art. 5 PCT for the following reasons:
- claims 7-9 relate to functional equivalents of PDK1, Ypk1/Ykr2, SGK and PKB without however, providing any indication as to other such equivalents than those mentioned earlier on;
 - claim 15 relates to a yeast cell which is capable of expressing a functional equivalent of Pkh1 and/or Pkh2: however the only such equivalent actually disclosed in the application is PDK1.
 - claim 28 is only supported / reproducible insofar as limited to Ypk1 and Ykr2 (i.e. if its subject-matter coincided with that of claim 29), since no other equivalents are disclosed in the application.
 - claim 30 lacks support since no yeast endogenous functional equivalents of Ypk1 and Ykr2 are disclosed.
- The lack of support for the subject-matter of these claims is such that no opinion as to novelty and inventive step can be given therefor.

PATENT COOPERATION TREATY

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REC'D 05 JAN 2001

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference MEDY/P22233PC	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB99/04228	International filing date (day/month/year) 14/12/1999	Priority date (day/month/year) 14/12/1998
International Patent Classification (IPC) or national classification and IPC C12Q1/00		
Applicant [THORNER, Jeremy William et al.] Medical Research Council.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 14 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none">I <input checked="" type="checkbox"/> Basis of the reportII <input type="checkbox"/> PriorityIII <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicabilityIV <input type="checkbox"/> Lack of unity of inventionV <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statementVI <input type="checkbox"/> Certain documents citedVII <input checked="" type="checkbox"/> Certain defects in the international applicationVIII <input checked="" type="checkbox"/> Certain observations on the international application		
Date of submission of the demand 10/07/2000	Date of completion of this report 02.01.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Luzzatto, E Telephone No. +49 89 2399 8169	



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/04228

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

Description, pages:

1-123 as originally filed

Claims, No.:

1-30,32-49 as originally filed

Drawings, sheets:

1-19 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
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- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
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- ☐ the description, pages:
- ☐ the claims, Nos.:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/04228

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 7-9,15,23,27,31-43.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 33,34,36 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☒ the claims, or said claims Nos. 7-9,15,23,28,32 are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 27,31,35,37-43.

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims 1-6,10-12,16,20-22,47,49

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/04228

	No:	Claims	13,14,17-19,24-26,28-30,44-46,48
Inventive step (IS)	Yes:	Claims	11,12,16,20-22
	No:	Claims	1-6,10,13,14,17-19,24-26,28-30,44-49
Industrial applicability (IA)	Yes:	Claims	1-6,10-14,16-22,24-26,28-30,44-49
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/04228

Re Item I

Basis of the opinion

- 1) Sequence listing pages 1-39 filed with the letter of 12.4.2000 do not form part of the application (Rule 13^{ter}.1(f) PCT).

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

- 1) Claims 27, 35, 37-43 have not been searched: their subject-matter therefore has not been examined (R. 66.1(e) PCT) (see also part VIII hereinbelow).
- 2) Claims 7-9, 15, 23, 28, 32-34 has not been examined in view of lack of support (Art. 6) (see item VIII hereinbelow).
- 3) Claims 33, 34 and 36 has not been examined for lack of clarity (see item VIII.8 hereinbelow).
- 4) Claim 31 is not to be found in the claims on file.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: DNA, 469-474, 1988
- D2: Mol.Gen. Genet., 443-447, 1993
- D3: Gene, 177-180, 1989
- D4: Emfun (EMBL), Acc. Number Z74842
- D5: Trembl (EMBL), Acc. Number Q03407)
- D6: Yeast, 655-664, 5/98
- D7: WO-A-9423039

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/04228

- 1) The present application does not meet the requirements of Art. 33(2) PCT due to lack of novelty.
 - 1.1) D1 (DNA, Maurer et al.) and D2 (Chen et al., MGG) disclose the Ypk1 protein kinase, which is capable of phosphorylating the polypeptide defined in claim 24 as well as being phosphorylated by Pkh1 or Pkh2 or PDK1. D1 and D2, therefore, anticipate the subject-matter of claims 24-26.
D3 (Gene, Kubo et al.) discloses the yeast YKR2 protein kinase. Also this document, thus, anticipates the subject-matter of claims **24-26**.
 - 1.2) D4 (Z74842) and D5 (Q03407) disclose the polypeptide encoded by the ORF YOL100w and that having the sequence designated in the application as SEQ ID 47 (p. 15, l. 20-p. 16, l. 6 of the description) respectively, thus anticipating the subject-matter of claims **44, 45 and 48** (as to the latter, it should be noted that for the assessment of novelty what matters are the actual features of the product, independent of the way in which the product has been obtained).
 - 1.3) D2 discloses *S. cerevisiae* mutants unable to express functional Ypk1 or Ypk2 kinases. It thus anticipates the subject-matter of claims **28-30** (see also item VIII.9 hereinbelow).
 - 1.4) D6 (Yeast, Bisland et al.) discloses yeast cells whose ORF YOL100w has been disrupted by insertion of a selectable marker (see abstract, Material and Methods, chapter "Genomic disruptions", fig.1, p. 662, left-hand col., l. 9-p. 663, right-hand col., l. 31). It also discloses the transformation of cells with the entire disruption insert (see chapter "plasmid construction" starting on p. 658).
D6, thus, anticipates the subject-matter of claims **13, 14, 17-19, 46**.
- 2) The present application does not meet the requirements of Art. 33(3) PCT due to lack of an inventive step.
 - 2.1) D7 (WO-A-9423039) is considered to represent the closest prior art.
It discloses a screening method for an inhibitor of a mammalian protein kinase

(PK) comprising the transformation of a yeast cell (e.g. *S. pombe*) with the mammalian gene coding for the said PK, wherein the yeast cell is incapable of expressing the yeast gene equivalent to the mammalian PK (see passages cited in the Search Report). As clearly shown by examples 4 and 5, the screening method comprises the use of the aforescribed transformed strain along with a non-transformed control strain (which corresponds to the "first host cell" to which claim 1 relates).

Hence, the sole difference between the method of D7 and that of claim 1 is that the latter excludes the use of a mammalian gene for transformation or uses a pathogenic yeast.

However, absent any indication whatsoever as to an unexpected effect linked to the use of a non-mammalian gene/pathogenic yeast or as to e.g. a prejudice in the art which would have prevented the skilled person from extending the teaching of D7 to non-mammalian genes or to pathogenic yeasts, the subject-matter of claims 1 and 2 appears to be the mere result of the customary practice of the skilled person.

Moreover, it is not even clear which (if any) is the technical problem solved by the general methods of claims 1 and 2; a screening assay for the identification of a compound should be based on the clear identification of a target molecule, thus allowing the identification of specific compounds which affect the said target. In the present case, no such target is defined: the general class of protein kinase is too broad to be considered as a specific target.

Claims 1 and 2, thus, lacks an inventive step.

Even if this objection had been overcome, the claims would have still offended against Art. 5 and 6 (see part VIII.1 hereinbelow).

2.2) Dependent claims 3-5, 10 relate to well known yeast species and well known features and thus lack an inventive step (art. 33(3) PCT).

2.3) Claim 6 relates to Pkh1 and Pkh2, which are not disclosed in the prior art, if the objection under Art. 6 had been overcome (see item VIII hereinbelow), would have thus been novel (Art. 33(2) PCT).

However, an inventive step cannot be acknowledged for this claim, in view of the fact that Pkh1 and Pkh2 are the products of well known ORFs, which were known to code for PK. Hence, the mere use of known PK in a conventional assay is not

inventive.

- 2.3) No opinion can be given as to the novelty and inventive step of subject-matter of claims 7-9 (see item VIII hereinbelow).
- 2.4) If the clarity objection had been overcome (see item VIII hereinbelow) by limiting claims 11 and 12 to the systems (Pkh1+Pkh2)/PDK1 and (Ykp1 +Ykr2)/SGK, the subject-matter of these claims could have met the requirements of Art. 33 PCT since none of the documents cited in the Search Report discloses or suggests the functional equivalence of the two said pairs of proteins and PDK1 and SGK. Thus, assays for the identification of compounds based on these systems are neither disclosed nor suggested in the available prior art.
- 2.5) Claim 16 appears to meet the requirements of Art. 33 PCT (see however part VIII hereinbelow), since, absent any indication in the prior art as to the relatedness of Pkh1 and Pkh2 with PDK1, the skilled person would have had no incentive to produce a cell as claimed.
For the same reasons, claims 20, 21 and 22 appear to meet the requirements of Art. 33 PCT.
As to claim 23, an opinion as to novelty and inventive step could only have been given if the objection under Art. 5 and 6 PCT (see item VIII) had been overcome.
- 2.6) If the clarity objection had been overcome (see item VIII.1) by suitably limiting its subject-matter, claim 32 would lack an inventive step, because Ypk1 and Ykr2 are known PK and their substrates are known. The amended claim would be rendered novel by the disclaimer relating to SGK, PKB α and p70S6 kinase. However no inventive step could be acknowledged in view of the absence of any unexpected feature in the mere extension of known assays to the general class to which the known substrates belong.
- 2.7) If the clarity objection had been overcome (see item VIII) by clearly and unambiguously relating claim 33 to the proteins actually disclosed in the application, i.e. Pkh1 and Pkh2, the claimed subject-matter could have possibly met the requirements of Art. 33 PCT.
The same line of arguments applies to claim 34, which could have met the

requirements of Art. 33 PCT if **clearly and unambiguously** related to the use of PDK1 to phosphorylate Ypk1, Ykr2 or SGK.

- 2.8) In view of the fact that the polypeptides encoded by the ORF yol100w and YDR490c are known, as well as their function, no inventive step can be acknowledged for the subject-matter of claim 47 and 49. As to claim 49, this conclusion is further reinforced by the the absence of any indication that such an antibody has been obtained and, hence, of any unexpected features thereof.
- 3) The document CASAMAYOR A ET AL: Functional counterparts of mammalian protein kinases PDK1 and SGK in budding yeast.' CURRENT BIOLOGY, (1999 FEB 25) 9 (4) 186-97. , XP000909655 could become relevant should the priority of the present application not be valid.

Re Item VII

Certain defects in the international application

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D7 is not mentioned in the description, nor are these documents identified therein.

Re Item VIII

Certain observations on the international application

- 1) The claims lack clarity (Art. 6 PCT) due to the use of the term "equivalent" in the following context "...protein kinase... **equivalent to the said host yeast cell protein kinase...**", because it is not possible for the skilled person to clearly and unambiguously understand the meaning of the term "equivalent". The description provides a definition of the said term (p. 6), however it falls short of describing a test capable of identifying, **clearly and unambiguously**, a protein kinase equivalent to another one. This is especially true in view of the fact that protein kinase have a plethora of effects, and thus each single PK would require a specific test.
- This inherent ambiguity of the claimed method is also shown by the fact that claim

6 relates to Pkh1 or Pkh2 as the host yeast cell protein kinase to be used in the method of claim 1; however, as clearly disclosed in the application (p. 78, l. 15-p. 79, l. 12) single deletion mutants (pkh1 Δ and pkh2 Δ) are viable and grow indistinguishably from congenic PKH1⁺ and PKH2⁺ (see D8, p. 187, right-hand col., first full par.). The same applies to Ypk1 and Ykr2 (see aforementioned passages and p. 87-88).

Hence, the skilled person, on the basis of the application, is not even in the condition to come to the conclusion that Pkh1 or Pkh2 are functional equivalents of PDK1: he can only apparently conclude that **both** said proteins, considered as a single system, are equivalent to PDK1. The same applies to Ypk1 and Ykr2 with respect to SGK. Concerning PKB, the description states that only very high expression levels of the said protein could rescue inviable ypk Δ ykr2 Δ (p. 78, l. 23-27, p. 89, l. 2-5) and provides no indication that such a protein would be suitable for the claimed assay.

Claims 1 and 2 are thus unclear because the expression "functional equivalent" is vague.

The same applies to claims 13,15,16,18,19,28-30,32-34.

- 2) Moreover, the said claims contravene Art. 6 for lack of support and their subject-matter contravenes Art. 5 since a suitable test for determining a functional equivalent of any given protein kinase valid for the whole breadth of the claims is not disclosed in the application. The skilled person is only capable of reproducing the claimed method insofar as related to the systems (Pkh1 and Pkh2)/PDK1 and (Ypk1 and Ykr2)/SGK.

The absence of any indication as to the said equivalents entails that no opinion can be given as to novelty and inventive step for the subject-matter of claim 32, since such an opinion could only be limited to Ypk1 and Ykr2.

It should be stressed that the contribution the invention allegedly makes over the prior art is to be seen in the identification of the kinases Pkh1 and Pkh2 as functional equivalents of PDK1 and of Ypk1 and Ykr2 of SGK. In the present case, therefore, claims whose subject-matter does not directly relate to the said proteins would amount to an unwarranted extension of protection.

- 3) No Pkh1 and Pkh2/Ypk1 and Ykr2 pathogenic yeast equivalents are described in the application: example 4 allegedly relates to the "identification of Candida

genes" related to these genes, but it merely discloses fragments of three Candida genes which appear to be closely related thereto: no data of any kind (not even the full length sequence) are provided which could support the contention that the said equivalents have actually been identified. Example 4, therefore, merely indicates that said equivalents **could be found**. Hence, also concerning the use of pathogenic yeast in the claimed methods, the application contravenes Art. 5 and the claims lack support (Art. 6 PCT).

- 4) The polypeptide Pkh1 is defined as having the sequence designated SEQ ID 47 whereas Pkh2 is encoded by the sequence SEQ ID 42. No other yeast equivalent proteins are described in the application.
Hence all claims relating to undefined equivalent ORFs of Pkh1 and Pkh2 (namely cl. 6, 26 44 and claims directly or indirectly dependent thereon) should have been amended by deleting any reference thereto, in order for them to comply with the requirements of Art. 6 (support) and 5 PCT.
- 5) Claims 24 and 25 are unclear (Art. 6 PCT). The fact that kinases may have a higher phosphorylating efficiency for a certain sequence or a certain protein than for others does not necessarily entail that they are not capable to phosphorylate different substrates, albeit with a lower efficiency. Hence, claims 24 and 25 do not allow a clear and unambiguous definition of the matter for which protection is sought, in view of the fact that known kinases might well phosphorylate the substrates to which the claims relate.
The said claims should have thus been amended by introducing clear technical features of the claimed protein.
- 6) Claim 35 does not relate to any technical feature and contravenes therefore Art. 6 PCT for lack of clarity.
- 7) Claim 36 is dependent on claim 35 and relates to "said yeast cell protein...". It is thus unclear (Art. 6 PCT) since claim 35 does not relate to any protein kinase. Hence, since also claim 35 and claims 1 and 2 are unclear, claim 36 is so unclear that no opinion can be given as to novelty and inventive step.
- 8) Claims 33 and 34 are unclear (Art. 6 PCT) in view of the fact that the expression

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International application No. PCT/GB99/04228

"suitable variant, fragment, derivative or fusion thereof..." appears to encompass any possible protein, even not directly related to Ypk1, Ypk2 or SGK, such as PKB α and p70S6 kinase. Hence, since this expression is also used in combination with Pkh1/2 and PDK1 respectively, the claims do not clearly define either the phosphorylating or the phosphorylated agent, thus rendering impossible a clear definition of the matter for which protection is sought.

The same applies to claims 47 and 48, which can only be examined insofar as related to Pkh1 and Pkh2, i.e. to the products of the ORFs YOL100w and YDR490c.

- 9) The same argument set out as to claim 34 applies to claim 44, which thus also lacks clarity.

Moreover, claim 44 also lacks clarity due to the expression "equivalent ORF" which leaves the skilled person at a loss as to the exact scope of the claim. Claim 44 contravenes Art. 6 PCT also for lack of support, in view of the fact that it is only with undue burden that the skilled person could find out which, if any, ORFs are equivalent to the *S. Cerevisiae* ORFs to which the claim relates. That this task is no obvious one, is shown by one of the main basis for the present invention, i.e. the characterisation of the protein products (Pkh1 and Pkh2) encoded by a **known** ORF (see p. 91, l. 25-p. 92, l. 7 of the description). The same objection applies of course to claims 45-49 which are, directly or indirectly, dependent on claim 44.

- 10) Claims 37-43 are unclear in that they do not relate to any technical feature of the claimed compounds and should be thus deleted.

- 11) The lack of definite meaning of the expression "variant, derivative, fragment..." discussed in hereinabove renders fully unclear the scope of claim 27, which should thus be deleted.

- 12) The subject-matter of claim 30 is unclear for the following reasons:
- the expression "for example" renders the three proteins which follow it in the claim completely non-limiting, hence rendering the meaning of the claim fully unclear (see Guidelines, III, 4.6);
Moreover, the claim and its subject-matter contravene A. 6 (lack of support) and

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Art. 5 PCT respectively, in that the skilled person could reproduce the invention without undue burden only insofar as related to exemplified proteins, namely SGK, Ypk1, Ykr2. The description itself states that "such a method **may be used for the identification of a functional homologue of Ypk1 or Ykr2...**" (p. 54, l. 19-20), thus indicating that no such homologues are known.

- 13) Claim 32 lacks support (Art. 6 PCT) for the same reasons set out with respect to claim 30.
- 14) Even if claim 30 was interpreted by not taking into account the expression "for example", it contravenes in any case Art. 6 for lack of clarity, in that its subject-matter is broader than that of claims 28 and 29, on which it should depend (see Guidelines, III, 3.4-3.5).
- 15) Claim 1 is unclear (Art. 6 PCT) because the expression "pathogenic yeast" is meaningful only if the organism for which the yeast is pathogenic is defined.
- 16) Claim 11 is unclear (Art. 6 PCT) because the terms Pkh1 and Pkh2 are in brackets (point 1) and 2)), thus allowing the interpretation that they are but an example of a functional equivalent of PDK1. However, they are the only such equivalents known and the contribution the invention allegedly makes over the prior art is based on this very discovery. Hence, the claim should have been amended by clearly relating it to yeast cells incapable of expressing the Pkh1 and Pkh2 proteins, thus dispelling any doubt as to the meaning of the expression "functional equivalent of human PDK1".
- 15) Claim 14 is unclear, since Pkh1 and Pkh2 relate to well defined *S.cerevisiae* protein kinases, and no other proteins with this denomination appear to have been described in the prior art or in the application. Hence, the expression "...**endogenous** Pkh1 and/or Pkh2..." should have been deleted since it appears to entail that various Pkh1 and Pkh2 proteins are known.
- 16) The sequence designations to be found on p. 47, l. 23, 44, l. 21 are unclear. They should have been either clarified in their meaning or been deleted.

**INTERNATIONAL PRELIMINARY
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- 17) Claims 23 lacks support (Art. 6 PCT) and its subject-matter contravenes Art. 5 PCT since no further yeast equivalents of PDK1 are disclosed besides Pkh1 and Pkh2, especially no Candida equivalents. The said claim should have thus been deleted.
- 18) Claims 7-9, 15, 28, 30 lack support (Art. 6) and their subject-matter contravenes Art. 5 PCT for the following reasons:
- claims 7-9 relate to functional equivalents of PDK1, Ypk1/Ykr2, SGK and PKB without however, providing any indication as to other such equivalents than those mentioned earlier on;
 - claim 15 relates to a yeast cell which is capable of expressing a functional equivalent of Pkh1 and/or Pkh2: however the only such equivalent actually disclosed in the application is PDK1.
 - claim 28 is only supported / reproducible insofar as limited to Ypk1 and Ykr2 (i.e. if its subject-matter coincided with that of claim 29), since no other equivalents are disclosed in the application.
 - claim 30 lacks support since no yeast endogenous functional equivalents of Ypk1 and Ykr2 are disclosed.
- The lack of support for the subject-matter of these claims is such that no opinion as to novelty and inventive step can be given therefor.

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

06 September 2000 (06.09.00)

International application No.

PCT/GB99/04228

Applicant's or agent's file reference

MEDY/P22233PC

International filing date (day/month/year)

14 December 1999 (14.12.99)

Priority date (day/month/year)

14 December 1998 (14.12.98)

Applicant

THORNER, Jeremy, William et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

10 July 2000 (10.07.00)



in a notice effecting later election filed with the International Bureau on:

2. The election



was



was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Juan Cruz

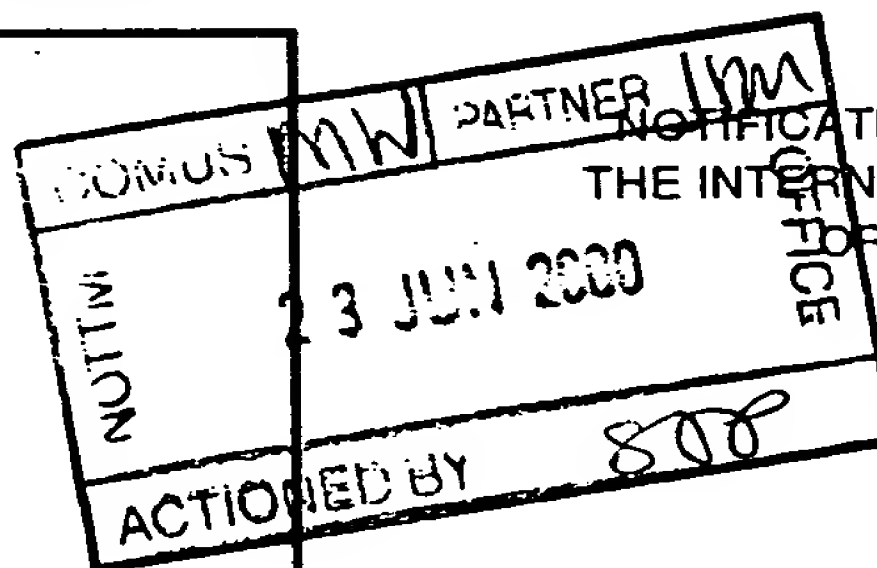
Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
ERIC POTTER CLARKSON
Attn. MILES, John S.
Park View House
58 The Ropewalk
Nottingham NG1 5DD
UNITED KINGDOM



NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
FOR THE DECLARATION

(PCT Rule 44.1)

Date of mailing
(day/month/year) 20/06/2000

Applicant's or agent's file reference
MEDW/P22233PC

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/GB 99/ 04228

International filing date
(day/month/year) 14/12/1999

Applicant

THORNER, Jeremy William et al.

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 551 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Josef Potsch

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference MEDW/P22233PC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 99/ 04228	International filing date (day/month/year) 14/12/1999	(Earliest) Priority Date (day/month/year) 14/12/1998
Applicant THORNER, Jeremy William et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

SCREENING METHODS BASED ON THE USE OF PROTEIN KINASES

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

1A

☒ as suggested by the applicant.

☐ None of the figures.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 99/04228

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 27, 35, 37-43
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 27,35,37-43

Claims 35 does not relate in a clear and unambiguous way to any technical feature which could allow a meaningful search with respect to the claimed kit to be carried out.

Claims 38-43 relate to a completely undefined subject-matter, since no compounds which could fall within the scope of the said claims have been disclosed in the application. Hence, no technical feature can be identified on which a meaningful search could be based.

Claim 37 relates to a protein kinase solely defined by its being novel; hence, no technical features are to be found in this claim which could provide a basis for a search.

Claim 44 relates to pure polypeptides encoded by an *S. cerevisiae* ORF which, however, are not defined by a sequence in a searchable format: the search has thus been carried out on the basis of *S. cerevisiae* sequences provided in the sequence listing, namely SEQ ID 42 and 48. The same applies to claims 45-49 which are, directly or indirectly, dependent on claim 44.

Claims 33 and 34 have been searched only insofar as related to the use of Pkh1/2 or PDK1 respectively to phosphorylate any protein, except (for PDK1) PKBalpha and p70S6 kinase, in view of the fact that the expression "suitable variant, fragment, derivative or fusion thereof..." appears to encompass any possible protein. This interpretation of the said expression is suggested by the disclaimer relating to proteins not directly related to Ypk1, Ypk2 or SGK as PKBalpha and p70S6. The undefined meaning of the said expression renders also a meaningful search with respect to the subject-matter of claim 27 impossible.

The invention is based on the discovery of two yeast equivalents of PDK1, namely Pkh1 and Pkh2: no other such equivalents are disclosed in the application or can be meaningfully searched. Hence, claim 11 has been searched only insofar as limited to Pkh1 and Pkh2 as functional equivalents of PDK1.

The invention is further based on the discovery that the yeast proteins Ypk1 and Ykr2 are the functional equivalents of the human protein kinase SGK. This is the contribution over the prior art that the invention could be seen as providing. No other such functional equivalents are disclosed in the application or can be searched for in a meaningful way. The search with respect to the subject-matter of claim 12, therefore, has been limited to a method wherein the yeast cell is incapable of expressing Ypk1 and/or Ykr2 and is capable of expressing SGK.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/39 C12N9/12 C12Q1/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMFUN [Online] EMBL, Heidelberg Accession Number Z74842 (Y13140), 9 July 1996 (1996-07-09) DURAND P. ET AL.: "S. cerevisiae chromosome XV reading frame ORF YOL100w" XP002138494 abstract	44
X	--- DATABASE TREMBL [Online] EMBL, Heidelberg Accession Number Q03407 (S. cerevisiae; pkinase), 1 November 1996 (1996-11-01) DIETRICH F.S. ET AL. : "Sequence from N.A." " XP002138495 abstract	44
	--- -/--	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

30 May 2000

Date of mailing of the international search report

12.06.00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Luzzatto, E

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	R.A.MAURER: "Isolation of a yeast protein kinase gene by screening with a mammalian protein kinase cDNA" DNA, vol. 7, 1988, pages 469-474, XP000886952 cited in the application the whole document ---	24-26
X	WO 94 23039 A (CANCER RES INST ROYAL ;MARSHALL CHRISTOPHER JOHN (GB); ASHWORTH AL) 13 October 1994 (1994-10-13) abstract; examples 4,5 page 4, line 1 - line 12 page 6, line 28 -page 11, line 23; claims ---	1
X	CHEN, PING ET AL: "A pair of putative protein kinase genes (YPK1 and YPK2) is required for cell growth in Saccharomyces cerevisiae." MOLECULAR & GENERAL GENETICS, (1993) VOL. 238, NO. 2-3, PP. 443-447. , XP000887391 the whole document ---	28-30
X	KUBO K. ET AL.: "A novel yeast gene coding for a putative protein kinase" GENE, vol. 76, 1989, pages 177-180, XP000887394 cited in the application the whole document ---	24-26
X	E. BILSLAND ET AL.: "Yeast functional analysis report" YEAST, vol. 14, no. 7, May 1998 (1998-05), pages 655-664, XP000909706 UK the whole document ---	13,14, 17-19
A	US 5 789 184 A (MANFREDI JOHN ET AL) 4 August 1998 (1998-08-04) column 7, line 50 -column 10, line 59 ---	1
A	EP 0 861 896 A (DADE BEHRING MARBURG GMBH) 2 September 1998 (1998-09-02) the whole document ---	28-34
A	WO 98 41638 A (MEDICAL RES COUNCIL) 24 September 1998 (1998-09-24) page 79, line 25 -page 81, line 14; claims; examples 6-14 ---	32

-/--

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ALESSI D R ET AL: "3-PHOSPHOINOSITIDE-DEPENDENT PROTEIN KINASE-1 (PK1): STRUCTURAL AND FUNCTIONAL HOMOLOGY WITH THE DROSOPHILA DSTPK61 KINASE" CURRENT BIOLOGY,GB,CURRENT SCIENCE,, vol. 7, no. 10, 1 October 1997 (1997-10-01), pages 776-789, XP002070054 ISSN: 0960-9822 the whole document	34
P,X	----- CASAMAYOR A ET AL: "Functional counterparts of mammalian protein kinases PK1 and SGK in budding yeast." CURRENT BIOLOGY, (1999 FEB 25) 9 (4) 186-97. , XP000909655 -----	13-19, 28-30, 33,34, 44-48

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.

PCT/GB 99/04228

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9423039	A	13-10-1994	AU 677834 B	08-05-1997
			AU 6382394 A	24-10-1994
			CA 2157774 A	13-10-1994
			EP 0703984 A	03-04-1996
			JP 9501302 T	10-02-1997
			US 5958721 A	28-09-1999
			AU 696939 B	24-09-1998
			AU 1586195 A	29-08-1995
			CA 2182967 A	17-08-1995
			EP 0742827 A	20-11-1996
			WO 9521923 A	17-08-1995
			JP 9508795 T	09-09-1997

US 5789184	A	04-08-1998	US 5876951 A	02-03-1999
			AU 6354198 A	09-07-1998
			AU 685103 B	15-01-1998
			AU 6490994 A	24-10-1994
			CA 2158274 A	13-10-1994
			EP 0692025 A	17-01-1996
			EP 0915154 A	12-05-1999
			JP 8510115 T	29-10-1996
			WO 9423025 A	13-10-1994

EP 0861896	A	02-09-1998	DE 19708173 A	03-09-1998
			CA 2224404 A	28-08-1998
			JP 10248566 A	22-09-1998

WO 9841638	A	24-09-1998	AU 6412498 A	12-10-1998
			EP 0983363 A	08-03-2000

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference MEDW/P22233PC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 99/ 04228	International filing date (day/month/year) 14/12/1999	(Earliest) Priority Date (day/month/year) 14/12/1998
Applicant THORNER, Jeremy William et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

SCREENING METHODS BASED ON THE USE OF PROTEIN KINASES

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

1A

☒ as suggested by the applicant.

☐ None of the figures.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 99/04228

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 27,35,37-43
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box 1.2

Claims Nos.: 27,35,37-43

Claims 35 does not relate in a clear and unambiguous way to any technical feature which could allow a meaningful search with respect to the claimed kit to be carried out.

Claims 38-43 relate to a completely undefined subject-matter, since no compounds which could fall within the scope of the said claims have been disclosed in the application. Hence, no technical feature can be identified on which a meaningful search could be based.

Claim 37 relates to a protein kinase solely defined by its being novel; hence, no technical features are to be found in this claim which could provide a basis for a search.

Claim 44 relates to pure polypeptides encoded by an *S. cerevisiae* ORF which, however, are not defined by a sequence in a searchable format: the search has thus been carried out on the basis of *S. cerevisiae* sequences provided in the sequence listing, namely SEQ ID 42 and 48. The same applies to claims 45-49 which are, directly or indirectly, dependent on claim 44.

Claims 33 and 34 have been searched only insofar as related to the use of Pkh1/2 or PDK1 respectively to phosphorylate any protein, except (for PDK1) PKBalpha and p70S6 kinase, in view of the fact that the expression "suitable variant, fragment, derivative or fusion thereof..." appears to encompass any possible protein. This interpretation of the said expression is suggested by the disclaimer relating to proteins not directly related to Ypk1, Ypk2 or SGK as PKBalpha and p70S6. The undefined meaning of the said expression renders also a meaningful search with respect to the subject-matter of claim 27 impossible.

The invention is based on the discovery of two yeast equivalents of PDK1, namely Pkh1 and Pkh2: no other such equivalents are disclosed in the application or can be meaningfully searched. Hence, claim 11 has been searched only insofar as limited to Pkh1 and Pkh2 as functional equivalents of PDK1.

The invention is further based on the discovery that the yeast proteins Ypk1 and Ykr2 are the functional equivalents of the human protein kinase SGK. This is the contribution over the prior art that the invention could be seen as providing. No other such functional equivalents are disclosed in the application or can be searched for in a meaningful way. The search with respect to the subject-matter of claim 12, therefore, has been limited to a method wherein the yeast cell is incapable of expressing Ypk1 and/or Ykr2 and is capable of expressing SGK.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/04228

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/39 C12N9/12 C12Q1/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMFUN 'Online! EMBL, Heidelberg Accession Number Z74842 (Y13140), 9 July 1996 (1996-07-09) DURAND P. ET AL.: "S. cerevisiae chomosome XV reading frame ORF YOL100w" XP002138494 abstract	44
X	DATABASE TREMBL 'Online! EMBL, Heidelberg Accession Number Q03407 (S. cerevisiae; pkinase), 1 November 1996 (1996-11-01) DIETRICH F.S. ET AL. : "Sequence from N.A." XP002138495 abstract	44



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

30 May 2000

Date of mailing of the international search report

20.06.00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Luzzatto, E

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/04228

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	R.A.MAURER: "Isolation of a yeast protein kinase gene by screening with a mammalian protein kinase cDNA" DNA, vol. 7, 1988, pages 469-474, XP000886952 cited in the application the whole document ---	24-26
X	WO 94 23039 A (CANCER RES INST ROYAL ;MARSHALL CHRISTOPHER JOHN (GB); ASHWORTH AL) 13 October 1994 (1994-10-13) abstract; examples 4,5 page 4, line 1 - line 12 page 6, line 28 -page 11, line 23; claims ---	1
X	CHEN, PING ET AL: "A pair of putative protein kinase genes (YPK1 and YPK2) is required for cell growth in Saccharomyces cerevisiae." MOLECULAR & GENERAL GENETICS, (1993) VOL. 238, NO. 2-3, PP. 443-447. , XP000887391 the whole document ---	28-30
X	KUBO K. ET AL.: "A novel yeast gene coding for a putative protein kinase" GENE, vol. 76, 1989, pages 177-180, XP000887394 cited in the application the whole document ---	24-26
X	E. BILSLAND ET AL.: "Yeast functional analysis report" YEAST, vol. 14, no. 7, May 1998 (1998-05), pages 655-664, XP000909706 UK the whole document ---	13,14, 17-19
A	US 5 789 184 A (MANFREDI JOHN ET AL) 4 August 1998 (1998-08-04) column 7, line 50 -column 10, line 59 ---	1
A	EP 0 861 896 A (DADE BEHRING MARBURG GMBH) 2 September 1998 (1998-09-02) the whole document ---	28-34
A	WO 98 41638 A (MEDICAL RES COUNCIL) 24 September 1998 (1998-09-24) page 79, line 25 -page 81, line 14; claims; examples 6-14 ---	32
	--- -/--	

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/04228

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ALESSI D R ET AL: "3-PHOSPHOINOSITIDE-DEPENDENT PROTEIN KINASE-1 (PK1): STRUCTURAL AND FUNCTIONAL HOMOLOGY WITH THE DROSOPHILA DSTPK61 KINASE" CURRENT BIOLOGY,GB,CURRENT SCIENCE,, vol. 7, no. 10, 1 October 1997 (1997-10-01), pages 776-789, XP002070054 ISSN: 0960-9822 the whole document</p>	34
P,X	<p>CASAMAYOR A ET AL: "Functional counterparts of mammalian protein kinases PK1 and SGK in budding yeast." CURRENT BIOLOGY, (1999 FEB 25) 9 (4) 186-97. , XP000909655</p>	13-19, 28-30, 33,34, 44-48

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/04228

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9423039 A	13-10-1994	AU 677834 B	08-05-1997
		AU 6382394 A	24-10-1994
		CA 2157774 A	13-10-1994
		EP 0703984 A	03-04-1996
		JP 9501302 T	10-02-1997
		US 5958721 A	28-09-1999
		AU 696939 B	24-09-1998
		AU 1586195 A	29-08-1995
		CA 2182967 A	17-08-1995
		EP 0742827 A	20-11-1996
		WO 9521923 A	17-08-1995
		JP 9508795 T	09-09-1997
US 5789184 A	04-08-1998	US 5876951 A	02-03-1999
		AU 6354198 A	09-07-1998
		AU 685103 B	15-01-1998
		AU 6490994 A	24-10-1994
		CA 2158274 A	13-10-1994
		EP 0692025 A	17-01-1996
		EP 0915154 A	12-05-1999
		JP 8510115 T	29-10-1996
		WO 9423025 A	13-10-1994
EP 0861896 A	02-09-1998	DE 19708173 A	03-09-1998
		CA 2224404 A	28-08-1998
		JP 10248566 A	22-09-1998
WO 9841638 A	24-09-1998	AU 6412498 A	12-10-1998
		EP 0983363 A	08-03-2000

U.S. APPL. NO. 09/808 118 INTERNATIONAL APPL. 0699/04228

APPLICATION FILED BY: 20 months _____ or 30 months ☒ Screening done by KW

INTERNATIONAL APPLICATION PAPERS IN THE APPLICATION FILE:

<input checked="" type="checkbox"/> International application (RECORD COPY) DOUBLE SIDED INTERNATIONAL APPLICATION <input checked="" type="checkbox"/> Article 19 amendments <input checked="" type="checkbox"/> PRIORITY DOCUMENT(S) NO. _____ <input checked="" type="checkbox"/> REQUEST FORM PCT/RO/101 <input checked="" type="checkbox"/> PCT/IB/302 <input checked="" type="checkbox"/> PCT/IB/306 (3) <input checked="" type="checkbox"/> PCT/IB/308 <input checked="" type="checkbox"/> PCT/IB/331 <input checked="" type="checkbox"/> OTHER: PCT/IB/_____ <input checked="" type="checkbox"/> PCT/IPEA/409 IPER (PCT/IPEA/416) <u>EP</u>	<input checked="" type="checkbox"/> 409 ANNEXES to IPER <input checked="" type="checkbox"/> PCT/ISA/210 (SEARCH REPORT) <u>EP</u> <input checked="" type="checkbox"/> Search Report References <input checked="" type="checkbox"/> Other papers filed WIPO PUBLICATION Publication No. <u>WO 01/36135</u> Publication Date <u>22 JUN 00</u> Publication Language <u>ENGLISH</u> <input checked="" type="checkbox"/> NOT PUBLISHED <input type="checkbox"/> U.S. only <input type="checkbox"/> Request
--	---

RECEIPT FROM THE APPLICANT: (other than checked above)

☒ SEQUENCE LISTING
☒ STATEMENT

<input checked="" type="checkbox"/> National Fee(paid or authorized to filed) <input checked="" type="checkbox"/> Express Processing Requested <input type="checkbox"/> Translation of International Application <input checked="" type="checkbox"/> Used the IB copy of International Application <input checked="" type="checkbox"/> Description <input checked="" type="checkbox"/> Claims no. <input checked="" type="checkbox"/> Drawings no. <u>19</u> <input type="checkbox"/> Foreign Language in drawing <input type="checkbox"/> Article 19 amendments <input type="checkbox"/> Amendments inserted into application <input type="checkbox"/> Article 34 amendments <input type="checkbox"/> Amendments inserted into application <input checked="" type="checkbox"/> DNA disk	<input checked="" type="checkbox"/> Preliminary amendment(s) filed <u>DATE 26 SEP 01</u> Second submission _____ <input type="checkbox"/> Information Disclosure Statement Second submission _____ <input type="checkbox"/> Assignment document forward to Assignment branch _____ <input type="checkbox"/> Substitute Specification _____ <input type="checkbox"/> Small Entity Statement _____ Type _____ <input type="checkbox"/> Oath/Declaration <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> Has the Oath/Declaration been executed <input type="checkbox"/> Power of Attorney/Change of address _____
--	--

35 U.S.C. 371 - Receipt of Request (PTO - 1309 Transmittal letter)	DATE: <u>14 JUN 01</u>
Date acceptable oath/declaration received	<u>26 SEP 01</u>
Date complete 35 U.S.C. 371 requirements met	
102 (e) Date	
DO/EO 903 Date of completion of Notification of Acceptance	
DO/EO 905 Date of completion of Notification of Missing Requirements	<u>23 JUL 01</u>
DO/EO 917 Date of completion of Notification of A Defective Oath or Declaration	
DO/EO 916 date of completion of Notification of Defective Response	<u>17 DEC 01</u>
DO/EO 913 Date of Notice of Defective Translation	
DO/EO 909 Date of Notification of Abandonment	<u>19 NOV 02</u>